

Claims:

1. A method for the diagnosis of a polymorphism in uPAR in a human, which method comprises determining either the sequence of the nucleic acid of the human at one or more of positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953, or the sequence of the amino acid in the uPAR protein at positions 198 or 295, and determining the status of the human by reference to polymorphism in the uPAR gene or protein.

2. A method according to claim 1 in which the single nucleotide polymorphism, according to the position of the reverse complement of EMBL Accession Number AC006953, at position 14935 in the promoter region is presence of A and/or G; at position 15282 in the 5' UTR is presence of G and/or A; at position 19985 near exon 3 is presence of G and/or C; at position 20258 near exon 3 is presence of G and/or A; at position 33251 in exon 6 is presence of A and/or G; at position 36468 in the exon 7 is the presence of C and/or T; at position 36623 in exon 7 is presence of T and/or C; and, at position 36720 in the 3'UTR is presence of G and/or A.

3. A method as claimed in claim 1 or 2, wherein the nucleic acid region containing the potential single nucleotide polymorphism is amplified by polymerase chain reaction prior to determining the sequence.

4. A method as claimed in any of claims 1 - 3, wherein the presence or absence of the single nucleotide polymorphism is detected by reference to the loss or gain of, optionally engineered, sites recognised by restriction enzymes.

5. A method according to claim 1 or claim 2, in which the sequence is determined by a method selected from ARMS-allele specific amplification, allele specific hybridisation, oligonucleotide ligation assay and restriction fragment length polymorphism (RFLP).

6. A method according to claim 1 wherein the presence of a polymorphic amino acid residue in the uPAR protein is determined by immunological methods such as enzyme linked immunosorbent assay (ELISA).

7. A method as claimed in any of the preceding claims for use in assessing the predisposition and/or susceptibility of an individual to diseases mediated by uPAR ligands.

8. A method for the diagnosis of uPAR ligand-mediated disease, which method comprises:

obtaining sample nucleic acid from an individual;
detecting the presence or absence of a variant nucleotide at one or more of positions: 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953; and,
determining the status of the human by reference to polymorphism in uPAR.

9. A method for the diagnosis of uPAR ligand-mediated disease, which method comprises:

obtaining a protein containing sample from an individual;
detecting the presence or absence of a variant uPAR polypeptide on the basis of the presence of a polymorphic amino acid at either or both amino acid positions: 198 and 295; and,
determining the status of the human by reference to the presence or absence of a polymorphism in uPAR.

10. An isolated nucleic acid comprising any one of the following polymorphism containing sequences: the nucleic acid sequence of SEQ ID NO:1 with G at position 16; the nucleic acid sequence of SEQ ID NO:2 with A at position 16; the nucleic acid sequence of SEQ ID NO:3 with C at position 16; the nucleic acid sequence of SEQ ID NO:4 with A at position 16; the nucleic acid sequence of SEQ ID NO:5 with G at position 16; the nucleic acid sequence of SEQ ID NO:6 with T at position 16; the nucleic acid sequence of SEQ ID NO:7 with C at position 16; the nucleic acid sequence of SEQ ID NO:8 with A at position 16, or a complementary strand thereof.

11. A diagnostic nucleic acid primer capable of detecting a polymorphism in the uPAR gene at one or more of positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953.

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12. A diagnostic primer as claimed in claim 11 which is an allele specific primer adapted for use in ARMS.

13. An allele-specific oligonucleotide probe capable of detecting a polymorphism in the NK2R gene at one or more of positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953.

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14. An allele specific nucleotide probe which comprises the sequence disclosed in any one of SEQ ID Nos: 1 - 8 or 15 - 22, or a sequence complementary thereto.

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15. A diagnostic kit comprising one or more diagnostic primer(s) as defined in claim 11 or 12 and/or one or more allele-specific oligonucleotide probes(s) as defined in claim 13 or 14.

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16. A method of treating a human in need of treatment with a uPAR ligand antagonist drug in which the method comprises:
diagnosis of a single nucleotide polymorphism in uPAR gene in the human, which diagnosis comprises determining the sequence of the nucleic acid at one or more of positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953;
determining the status of the human by reference to polymorphism in the uPAR gene; and, administering an effective amount of a uPAR ligand antagonist.

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17. A method of treating a human in need of treatment with a uPAR ligand antagonist drug in which the method comprises:
diagnosis of a polymorphism in uPAR protein in the human, which diagnosis comprises determining the amino acid one or both of positions: 198 and 295 of the uPAR protein;

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determining the status of the human by reference to polymorphism in the uPAR protein; and, administering an effective amount of a uPAR ligand antagonist.

18. Use of an uPAR ligand antagonist drug in preparation of a medicament for treating a uPAR ligand mediated disease in a human diagnosed as having a particular single nucleotide polymorphism at one or more of positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953.
19. a pharmaceutical pack comprising an uPAR antagonist drug and instructions for administration of the drug to humans diagnostically tested for a single nucleotide polymorphism at one or more of positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, each defined by the position of the reverse complement of EMBL Accession Number AC006953.
20. A computer readable medium having stored thereon a nucleic acid sequence comprising at least 17, preferably at least 20 consecutive bases of the uPAR gene sequence, which sequence includes at least one of the polymorphisms at positions: 14935, 15282, 19985, 20258, 33251, 36468, 36623 and 36720, according to the position of the reverse complement of EMBL Accession Number AC006953.
21. A computer readable medium having stored thereon a nucleic acid sequence comprising at least 17, preferably at least 20 consecutive bases of the uPAR gene sequence, which sequence includes at least one of the following polymorphisms: G at position 14935, A at position 15282, C at position 19985, A at position 20258, G at position 33251, T at position 36468, C at position 36623 and A at position 36720, or a complementary strand thereof.
22. A computer readable medium having stored thereon a nucleic acid sequence comprising any of the sequences of SEQ ID No. 15 to SEQ ID No. 22, or a complementary sequence thereto.